is the case then there is the exciting prospect of a gene, perhaps responsible for specific amplifications, in an organism whose genetics are the envy of the eukaryotes.

LAMBDA PHAGE

How Gene *N* Works

from our Cell Biology Correspondent

IT seems to be inevitable that as molecular biologists probe deeper and deeper into the biology of this or that phage or into the chemistry of some biosynthetic process their work becomes increasingly inaccessible to their colleagues not least because of the artificial barriers which arise as jargons evolve. Lambdologists, whose discoveries have laid bare in extraordinary and fascinating detail the complicated biology of bacteriophage lambda, may seem particularly prone to lapse into a shorthand language which rapidly becomes almost totally incomprehensible to the outsider. But more often than not what they have to say is of general significance.

The elegant experiments of Georgopoulos reported in the current issue of the *Proceedings of the US National Academy of Sciences* (**68**, 2977 ; 1971) are a case in point. When a phage infects *Escherichia coli* it faces the problem of expressing its genetic information in a regulated way using, initially at least, the host cell's RNA polymerase to transcribe early phage messenger RNAs. Phage-like T7 and T3 apparently specify soon after infection a completely new RNA polymerase which specifically transcribes the late phage genes, something which the host enzyme is apparently incapable of doing. Phage T4, on the other hand, seems to achieve the same end by modifying the RNA polymerase of the host cell and by making a new sigma factor to subvert the cell's enzyme to the transcription of the phage chromosome. How does lambda phage solve this problem? It has been known for many years that the *N* gene of λ provides a positive regulatory element, without which the phage cannot express most of its genome and complete its replication cycle. Clearly the *N* gene product might be a new RNA polymerase, or it might somehow modify the host polymerase, or it might act not on the polymerase but on some other part of the transcription machinery. The experiments which Georgopoulos reports strongly indicate that the *N* gene product acts in the second of these three possible ways.

Georgopoulos has isolated a suite of mutant bacteria which do not support the complete replication of wild type λ and has shown that at least some of these mutants are growth minus (*gro*$^-$) because they prevent the *N* gene from functioning (*groN*$^-$). For example, λ *tryp* phage, which carry the *E. coli* tryptophan synthesis genes, can make tryptophan enzymes if the *N* gene of the phage can act normally. In other words, the amount of tryptophan enzymes made is a measure of the extent of *N* gene function. When *groN*$^-$ cells are infected with λ tryp the phage fails to replicate and it also fails to specify the tryptophan enzymes. Apparently, the *groN*$^-$ mutation in the host genome results in a modification of the target of the phage's *N* gene product such that this target molecule is no longer susceptible to attack by the *N* gene product. And by using *groN*$^-$ cells Georgopoulos has succeeded in isolating mutant λ phage which manage to replicate in *groN*$^-$ cells; these phage mutants fall into two classes, phage which, because of a deletion, have lost their requirement for *N* gene activity, and a second, more interesting class of phages which carry a mutation in their *N* gene which alters the *N* gene product and allows it to interact with the altered target in *groN*$^-$ cells. The mutation in the *N* gene, in other words, compensates for the *groN*$^-$ mutation in the cell's genome.

But what is the cellular target of the *N* gene product which is changed by the *groN*$^-$ mutation? By transduction experiments Georgopoulos showed that *groN*$^-$ mutations are very closely linked to the locus which confers resistance to rifamycin. This locus is known to specify one of the subunit polypeptides of RNA polymerase; perhaps therefore the *groN*$^-$ mutations are also in a locus which specifies part of the host's RNA polymerase. Georgopoulos therefore isolated RNA polymerase from wild type and *groN*$^-$ *E. coli* and showed that *in vitro* the two enzymes do indeed differ in their response to changing ionic strength and in their sensitivity to inhibition by rifamycin.

There seems little doubt that the *groN*$^-$ mutation changes *E. coli* RNA polymerase and it follows therefore that the host enzyme is in all probability the target of the *N* gene product. The question now, of course, is what does the *N* gene product do to RNA polymerase? Does it render the enzyme capable of initiating transcription at previously inaccessible sites on the genome or does it cause the enzyme to fail to respond to termination signals which in the absence of *N* gene product curtail transcription of most of the λ genome?

Heterogeneous Precursors to Ribosomal RNAs

THE genomes of plants and animals contain anything from about 200 to about 30,000 copies of the genes which specify ribosomal RNAs and as far as can be judged in each species these multiple copies are all identical. A structural gene for 18S ribosomal RNA (rRNA) and a structural gene for 28S rRNA are transcribed into a single long polycistronic RNA precursor molecule which, as is now known, is cut by a series of specific nucleolytic cleavages to yield the mature rRNAs and so-called spacer sequences which are apparently discarded. For reasons that are obscure, the amount of excess spacer RNA seems to be correlated with the organism's evolutionary position. There is more of it in warm blooded animals than in lower vertebrates, for example, and as Grierson and Loening suggest in next Wednesday's *Nature New Biology* (January 19), even within one organism the amount of spacer RNA transcribed may vary from tissue to tissue.

By gel electrophoresis Grierson and Loening analysed the maturation of ribosomal RNA in leaves and roots of the mung bean, *Phaseolus aureus*, and reach the conclusion that the largest preribosomal RNA that can be detected in the leaf is about 600 nucleotides larger than that in the root. Although definitive proof that the primary product of transcription in leaf and root differs in length depends on finger print analyses, and even then it will be hard to eliminate absolutely the possibility that in the root the transcript RNA is cleaved before its synthesis is completed, their data, together with the report of Tiollais *et al.* that precursor ribosomal RNA in mammalian cells is heterogeneous (*Proc. US Nat. Acad. Sci.*, **68**, 1117; 1971), strongly suggest that identical RNA genes in different tissues of the same organism may be differently transcribed. If this is the case there must presumably be two or more initiation or termination sites for RNA polymerase in each ribosomal RNA transcriptional unit.

Also in next Wednesday's *Nature New Biology* van der Helm and Krakow report experiments which suggest how steptolydigin inhibits RNA polymerase of *Escherichia coli*. This antibiotic blocks both the initiation of new RNA chains and the elongation of chains already initiated. Van der Helm and Krakow believe their experiments show that it freezes or stabilizes the complex of RNA polymerase and its template so as to distort the enzyme. As a result, they suggest, the orientation of the 3′ hydroxyl group at the growing end of the RNA chain is altered such that it can no longer react to form a diester bond with the phosphate residues at the 5′ position of the incoming nucleoside triphosphate and so transcription ceases, as does the translocation of the enzyme along its template.